

and having an IC_{50} of 100 μM or lower for inhibiting poly(ADP-ribose) polymerase *in vitro*,
or a pharmaceutically acceptable base or acid addition salt, prodrug, metabolite, optical isomer or
stereoisomer thereof, wherein:

X is double-bonded oxygen or -OH;

R^7 , when present, is hydrogen;

Y represents the atoms necessary to form a fused phenyl, pyridine, or pyrimidine ring;

and

Z is $-R^6C=CR^3-$ wherein R^6 and R^3 , taken together, form a fused phenyl, pyridine, or
pyrimidine ring;

wherein said fused phenyl, pyridine, or pyrimidine ring of Y or Z is independently
unsubstituted or substituted with at least one non-hydrogen, non-interfering substituent;
and

when the Y and Z rings are phenyl and X is double bonded oxygen, at least one of the Y
and Z rings contains at least one said substituent.

✓ 185. The method of claim 184, wherein X is double-bonded oxygen.

186. The method of claim 184, wherein Y has at least one site of unsaturation.

187. The method of claim 184, wherein Y represents the atoms necessary to form a fused benzene or naphthalene ring.

188. The method of claim 184, wherein Y is substituted with at least one non-hydrogen, non-interfering substituent.

Q1 189. The method of claim 184 wherein said substituent is selected from the group consisting of an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, an aryl, an alkoxy, an alkenoxy, an aryloxy, an aralkyloxy, an alkanoyl, a haloalkyl, a heterocyclic group, a heteroaryl, a halo group, hydroxy, carboxy, carbonyl, amino, an alkylamino, amido, cyano, isocyano, nitro, nitrilo, isonitrilo, nitroso, imino, azo, diazo, sulfonyl, sulfoxy, SO₃K, thio, thiocarbonyl, alkylthio and sulfhydryl.

190. The method of claim 184, wherein:

X is double bonded-oxygen;

Y is a fused benzene ring optionally substituted with a nitro group, an alkyl, an amino group, a halo group, a hydroxy, or a nitroso group; and

Z is -R⁶C=CR³- where R³ and R⁶, taken together, form a fused phenyl ring substituted with a substituent selected from the group consisting of a halo group, a nitro group, an alkyl, an amino group, a hydroxy, or a nitroso group.

191. The method of claim 184, wherein said compound has an IC_{50} for inhibiting poly(ADP-ribose) polymerase *in vitro* of 10 μM or lower.

192. The method of claim 184, wherein said compound has an IC_{50} for inhibiting poly(ADP-ribose) polymerase *in vitro* of 25 μM or lower.

X 193. The method of claim 184, wherein said compound is 5(*H*)2-chloro-10-methylphenanthridin-6-one.

ai X 194. The method of claim 184, wherein said compound is 5(*H*)2-nitro-10-methylphenanthridin-6-one.

X 195. The method of claim 184, wherein said compound is 5(*H*)2-chloro-10-aminophenanthridin-6-one.

✓ 196. The method of claim 184, wherein said compound is 5(*H*)2-nitro-10-aminophenanthridin-6-one.

X 197. The method of claim 184, wherein said compound is 5(*H*)2-chloro-10-nitrophenanthridin-6-one.

X 198. The method of claim 184, wherein said compound is 5(*H*)2,10-dinitrophenanthridin-6-one.

X 199. The method of claim 184, wherein said compound is 5(*H*)2-chloro-10-hydroxyphenanthridin-6-one.

X 200. The method of claim 184, wherein said compound is 5(*H*)2-nitro-10-hydroxyphenanthridin-6-one.

X 201. The method of claim 184, wherein said compound is 5(*H*)2-chloro-10-bromophenanthridin-6-one.

Q1 X 202. The method of claim 184, wherein said compound is 5(*H*)2-nitro-10-bromophenanthridin-6-one.

X 203. The method of claim 184, wherein said compound is 5(*H*)2-chloro-10-nitrosophenanthridin-6-one.

X 204. The method of claim 184, wherein said compound is 5(*H*)2-chloro-9,10-methlenedihydroxyphenanthridin-6-one.

X 205. The method of claim 184, wherein said compound is 5(*H*)2-nitro-9,10-methlenedihydroxyphenanthridin-6-one.

206. The method of claim 184, wherein said composition is in the form of a capsule or tablet containing a single or divided dose of said compound, wherein said dose is sufficient to prevent or reduce the effects of vascular stroke or other neurodegenerative disease.

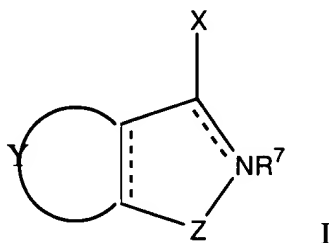
112 207. The method of claim 184, wherein said composition is administered as a sterile solution, suspension or emulsion, in a single or divided dose.

lack antecedent

208. The method of claim 184, wherein said composition is administered as a solid implant capable of releasing the compound over a prolonged period of time.

Q1 209. The method of claim 184, wherein said compound is present in an amount sufficient to treat or prevent neural tissue damage resulting from cerebral ischemia and reperfusion injury.

210. A method of effecting a neuronal activity in a mammal comprising administering to said mammal an effective amount of a compound of formula I containing at least one ring nitrogen:



and having an IC_{50} of 100 μM or lower for inhibiting poly(ADP-ribose) polymerase *in vitro*,

or a pharmaceutically acceptable base or acid addition salt, prodrug, metabolite, optical isomer or stereoisomer thereof, wherein:

X is double-bonded oxygen or -OH;

R⁷, when present, is hydrogen;

Y represents the atoms necessary to form a fused phenyl, pyridine, or pyrimidine ring;

and

Z is -R⁶C=CR³- wherein R⁶ and R³, taken together, form a fused phenyl, pyridine, or pyrimidine ring;

wherein said fused phenyl, pyridine, or pyrimidine ring of Y or Z is independently unsubstituted or substituted with at least one non-hydrogen, non-interfering substituent.

211. The method of claim 210, wherein the neuronal activity is not mediated by NMDA.

212. The method of claim 210, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.

213. The method of claim 212, wherein said neuronal activity is stimulation of damaged neurons resulting from cerebral ischemia or reperfusion injury.

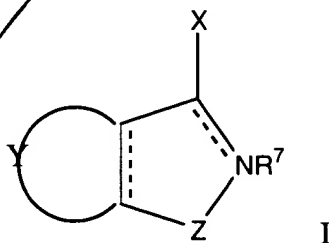
214. The method of claim 212, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic

brain injury, physical damage to the spinal cord, stroke associated with brain damage, demyelinating disease and neurological disorder relating to neurodegeneration.

X 215. The method of claim 214, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis.

a, 216. The method of claim 210 wherein said substituent is selected from the group consisting of an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, an aryl, an alkoxy, an alkenoxy, an aryloxy, an aralkyloxy, an alkanoyl, a haloalkyl, a heterocyclic group, a heteroaryl, a halo group, hydroxy, carboxy, carbonyl, amino, an alkylamino, amido, cyano, isocyano, nitro, nitrilo, isonitrilo, nitroso, imino, azo, diazo, sulfonyl, sulfoxy, SO₃K, thio, thiocarbonyl, alkylthio and sulfhydryl.

Sub B, duplicate with claim 216
217. A method of effecting a neuronal activity in a mammal comprising administering to said mammal an effective amount of a compound of formula I containing at least one ring nitrogen:



and having an IC₅₀ of 100 μ M or lower for inhibiting poly(ADP-ribose) polymerase *in vitro*,

or a pharmaceutically acceptable base or acid addition salt, prodrug, metabolite, optical isomer or stereoisomer thereof, wherein:

X is double-bonded oxygen or -OH;

R⁷, when present, is hydrogen;

Y represents the atoms necessary to form a fused phenyl, pyridine, or pyrimidine ring;

and

Z is -R⁶C=CR³- wherein R⁶ and R³, taken together, form a fused phenyl, pyridine, or pyrimidine ring;

wherein said fused phenyl, pyridine, or pyrimidine ring of Y or Z is independently unsubstituted or substituted with at least one non-hydrogen, non-interfering substituent.

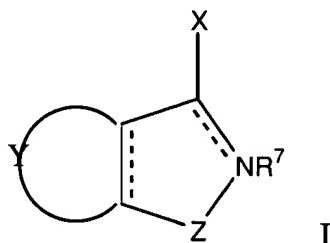
X 218. The method of claim 217, wherein said inflammation is colitis.

X 219. The method of claim 217, wherein said inflammation is Crohn's disease.

duplicate 216

220. The method of claim 217 wherein said substituent is selected from the group consisting of an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, an aryl, an alkoxy, an alkenoxy, an aryloxy, an aralkyloxy, an alkanoyl, a haloalkyl, a heterocyclic group, a heteroaryl, a halo group, hydroxy, carboxy, carbonyl, amino, an alkylamino, amido, cyano, isocyano, nitro, nitrilo, isonitrilo, nitroso, imino, azo, diazo, sulfonyl, sulfoxy, SO₃K, thio, thiocarbonyl, alkylthio and sulfhydryl.

221. A method of treating a cardiovascular disorder in a mammal comprising
Note
administering to said mammal an effective amount of a compound of formula I containing at least one ring nitrogen:



A1
and having an IC₅₀ of 100 μ M or lower for inhibiting poly(ADP-ribose) polymerase *in vitro*,
or a pharmaceutically acceptable base or acid addition salt, prodrug, metabolite, optical isomer or
stereoisomer thereof, wherein:

X is double-bonded oxygen or -OH;

R⁷, when present, is hydrogen;

Y represents the atoms necessary to form a fused phenyl, pyridine, or pyrimidine ring;

and

Z is -R⁶C=CR³ - wherein R⁶ and R³, taken together, form a fused phenyl, pyridine, or
pyrimidine ring;

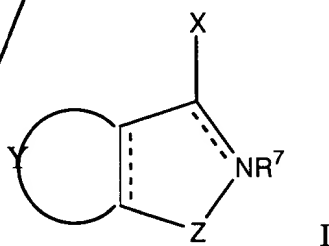
wherein said fused phenyl, pyridine, or pyrimidine ring of Y or Z is independently
unsubstituted or substituted with at least one non-hydrogen, non-interfering substituent.

222. The method of claim 221 wherein said substituent is selected from the group
consisting of an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, an aryl, an alkoxy, an
alkenoxy, an aryloxy, an aralkyloxy, an alkanoyl, a haloalkyl, a heterocyclic group, a heteroaryl,
a halo group, hydroxy, carboxy, carbonyl, amino, an alkylamino, amido, cyano, isocyano, nitro,

nitriilo, isonitriilo, nitroso, imino, azo, diazo, sulfonyl, sulfoxy, SO₃K, thio, thiocarbonyl, alkylthio and sulfhydryl.

223. The method of claim 221, wherein said cardiovascular disorder is selected from the group consisting of coronary artery disease, angina pectoris, myocardial infarction, cardiogenic shock, and cardiovascular tissue damage.

duplicate with claim 224
224. A method of effecting a neuronal activity in a mammal comprising administering to said mammal an effective amount of a compound of formula I containing at least one ring nitrogen:



and having an IC₅₀ of 100 μ M or lower for inhibiting poly(ADP-ribose) polymerase *in vitro*, or a pharmaceutically acceptable base or acid addition salt, prodrug, metabolite, optical isomer or stereoisomer thereof, wherein:

X is double-bonded oxygen or -OH;

R⁷, when present, is hydrogen;

Y represents the atoms necessary to form a fused phenyl, pyridine, or pyrimidine ring;

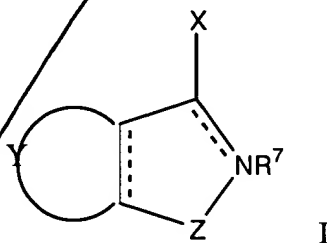
and

Z is $-R^6C=CR^3-$ wherein R^6 and R^3 , taken together, form a fused phenyl, pyridine, or pyrimidine ring;
wherein said fused phenyl, pyridine, or pyrimidine ring of Y or Z is independently unsubstituted or substituted with at least one non-hydrogen, non-interfering substituent.

21
225. The method of claim 224 wherein said substituent is selected from the group consisting of an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, an aryl, an alkoxy, an alkenoxy, an aryloxy, an aralkyloxy, an alkanoyl, a haloalkyl, a heterocyclic group, a heteroaryl, a halo group, hydroxy, carboxy, carbonyl, amino, an alkylamino, amido, cyano, isocyano, nitro, nitrilo, isonitrilo, nitroso, imino, azo, diazo, sulfonyl, sulfoxy, SO_3K , thio, thiocarbonyl, alkylthio and sulfhydryl.

226. The method of claim 224, wherein said septic shock is endotoxic shock.

227. A method of effecting a neuronal activity in a mammal comprising administering to said mammal an effective amount of a compound of formula I containing at least one ring nitrogen:



and having an IC_{50} of 100 μM or lower for inhibiting poly(ADP-ribose) polymerase *in vitro*,

or a pharmaceutically acceptable base or acid addition salt, prodrug, metabolite, optical isomer or stereoisomer thereof, wherein:

X is double-bonded oxygen or -OH;

R⁷, when present, is hydrogen;

Y represents the atoms necessary to form a fused phenyl, pyridine, or pyrimidine ring;

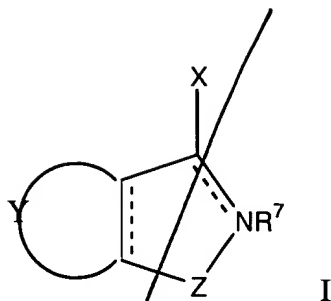
and

Z is -R⁶C=CR³- wherein R⁶ and R³, taken together, form a fused phenyl, pyridine, or pyrimidine ring;

wherein said fused phenyl, pyridine, or pyrimidine ring of Y or Z is independently unsubstituted or substituted with at least one non-hydrogen, non-interfering substituent.

duplicate 216
(228) The method of claim 227 wherein said substituent is selected from the group consisting of an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, an aryl, an alkoxy, an alkenoxy, an aryloxy, an aralkyloxy, an alkanoyl, a haloalkyl, a heterocyclic group, a heteroaryl, a halo group, hydroxy, carboxy, carbonyl, amino, an alkylamino, amido, cyano, isocyano, nitro, nitrilo, isonitrilo, nitroso, imino, azo, diazo, sulfonyl, sulfoxy, SO₃K, thio, thiocarbonyl, alkylthio and sulfhydryl.

duplicate 210
(229) A method of effecting a neuronal activity in a mammal comprising administering to said mammal an effective amount of a compound of formula I containing at least one ring nitrogen:



and having an IC_{50} of 100 μM or lower for inhibiting poly(ADP-ribose) polymerase *in vitro*,
or a pharmaceutically acceptable base or acid addition salt, prodrug, metabolite, optical isomer or
stereoisomer thereof, wherein:

X is double-bonded oxygen or -OH;

R^7 , when present, is hydrogen;

Y represents the atoms necessary to form a fused phenyl, pyridine, or pyrimidine ring;

and

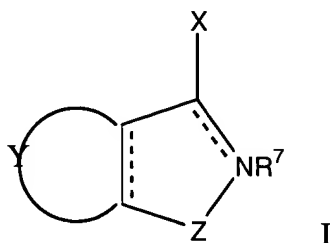
Z is $-R^6C=CR^3-$ wherein R^6 and R^3 , taken together, form a fused phenyl, pyridine, or
pyrimidine ring;

wherein said fused phenyl, pyridine, or pyrimidine ring of Y or Z is independently
unsubstituted or substituted with at least one non-hydrogen, non-interfering substituent.

duplicate 216
(230) The method of claim 229 wherein said substituent is selected from the group

consisting of an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, an aryl, an alkoxy, an
alkenoxy, an aryloxy, an aralkyloxy, an alkanoyl, a haloalkyl, a heterocyclic group, a heteroaryl,
a halo group, hydroxy, carboxy, carbonyl, amino, an alkylamino, amido, cyano, isocyano, nitro,
nitrilo, isonitrilo, nitroso, imino, azo, diazo, sulfonyl, sulfoxy, SO_3K , thio, thiocarbonyl, alkylthio
and sulfhydryl.

N₂₃₁. A method of treating cancer in a mammal comprising administering to said mammal an effective amount of a compound of formula I containing at least one ring nitrogen:



Q₁ and having an IC₅₀ of 100 μ M or lower for inhibiting poly(ADP-ribose) polymerase *in vitro*, or a pharmaceutically acceptable base or acid addition salt, prodrug, metabolite, optical isomer or stereoisomer thereof, wherein:

X is double-bonded oxygen or -OH;

R⁷, when present, is hydrogen;

Y represents the atoms necessary to form a fused phenyl, pyridine, or pyrimidine ring;

and

Z is -R⁶C=CR³- wherein R⁶ and R³, taken together, form a fused phenyl, pyridine, or pyrimidine ring;

wherein said fused phenyl, pyridine, or pyrimidine ring of Y or Z is independently unsubstituted or substituted with at least one non-hydrogen, non-interfering substituent;

and

when the Y and Z rings are phenyl and X is double bonded oxygen, at least one of the Y and Z rings contains at least one said substituent.

232. The method of claim 231 wherein said substituent is selected from the group consisting of an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, an aryl, an alkoxy, an alkenoxy, an aryloxy, an aralkyloxy, an alkanoyl, a haloalkyl, a heterocyclic group, a heteroaryl, a halo group, hydroxy, carboxy, carbonyl, amino, an alkylamino, amido, cyano, isocyano, nitro, nitrilo, isonitrilo, nitroso, imino, azo, diazo, sulfonyl, sulfoxy, SO₃K, thio, thiocarbonyl, alkylthio and sulfhydryl.

A1 233. The method of claim 231, wherein said cancer is selected from the group consisting of: ACTH-producing tumors, acute lymphocytic leukemia, acute nonlymphocytic leukemia, cancer of the adrenal cortex, bladder cancer, brain cancer, breast cancer, cervix cancer, chronic lymphocytic leukemia, chronic myelocytic leukemia, colorectal cancer, cutaneous T-cell lymphoma, endometrial cancer, esophageal cancer, Ewing's sarcoma, gallbladder cancer, hairy cell leukemia, head & neck cancer, Hodgkin's lymphoma, Kaposi's sarcoma, kidney cancer, liver cancer, lung cancer (small and/or non-small cell), malignant peritoneal effusion, malignant pleural effusion, melanoma, mesothelioma, multiple myeloma, neuroblastoma, non-Hodgkin's lymphoma, osteosarcoma, ovary cancer, ovary (germ cell) cancer, prostate cancer, pancreatic cancer, penis cancer, retinoblastoma, skin cancer, soft-tissue sarcoma, squamous cell carcinomas, stomach cancer, testicular cancer, thyroid cancer, trophoblastic neoplasms, cancer of the uterus, vaginal cancer, cancer of the vulva and Wilm's tumor.--

REMARKS

Reconsideration is requested.